Amendment #1 to RFP NIH-NIAID-DMID-00-18

"MALARIA VACCINE PRODUCTION AND SUPPORT SERVICES"

Request for Proposal No.:	NIH-NIAID-DMID-00-18
Amendment Number:	#1 (No other amendments have been issued.)
Amendment Issuance Date:	NOVEMBER 12, 1999
Amendment Issued to:	ALL POTENTIAL OFFERORS
RFP Issue Date:	Wednesday, September 15, 1999
Proposal Due Date:	Friday, January 14, 2000, 4:00 P.M (Unchanged)
Issued By:	Jacqueline C. Holden, NIAID, NIH Senior Contracting Officer Contract Management Branch 6700 B Rockledge Drive Room 2230, MSC 7612 Bethesda, Maryland 20892-7612
Point of Contact:	Nancy M. Hershey, Contracting Officer

The above numbered solicitation is amended as set forth below: The hour and date specified for receipt of offers is **NOT** extended. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram, letter or e-mail, provided each telegram, letter or e-mail makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.

PURPOSE: To provide information from the pre-proposal conference held on October 22, 1999, which includes the following: 1) an agenda of the meeting; 2) a record (including handouts) of the meeting; 3) a copy of the questions and answers concerning the RFP; and 4) a list of attendees.

Except as provided herein, all terms and conditions of the RFP document NIH-NIAID-DMID-00-18 remain unchanged and in full force and effect.

Offerors must acknowledge receipt of this amendment #1 prior to the offer/proposal due date and time specified in the solicitation or as amended, by one of the following methods:

1) By acknowledging receipt of the amendment on each copy of the offer submitted; or
2) By sending an electronic mail message to Nancy Hershey, Contract Specialist, at nh11x@nih.gov which includes a reference to the solicitation and amendment number; or
3) By sending the Contracting Officer a separate letter or telegram which includes a reference to the solicitation and amendment number.

Failure to receive your acknowledgement of this amendment prior to the hour and date specified for proposal receipt may result in the rejection of your offer.

Amendment #1 to RFP NIH-NIAID-DMID-00-18

1) Agenda for Pre-Proposal Conference on October 22, 1999

PRE-PROPOSAL CONFERENCE
6700 B ROCKLEDGE DRIVE
ROOM 1205
Bethesda, MD 20817
OCTOBER 22, 1999

RFP-NIH-NIAID-DMID-00-18
"MALARIA VACCINE PRODUCTION AND SUPPORT SERVICES"

AGENDA

9:00 AM

Introduction and Purpose of the Pre-Proposal Conference	Brenda Velez, Chief Contract Management Branch NIAID, NIH
Overview of the NIAID Malaria Vaccine Development Program	Stephanie James, Ph.D., Chief Parasitology & International Programs Branch Division of Microbiology And Infectious Diseases NIAID, NIH
Overview of the NIAID Malaria Vaccine Production and Support Services RFP	B. Fenton Hall, MD, Ph.D. Project Officer Parasite Vaccine Program Parasitology & International Programs Branch Division of Microbiology And Infectious Diseases NIAID, NIH
Carole Long Head of Immunology Malaria Vaccine Development Unit Lab of Parasitic Diseases NIAID, NIH	Anthony Stowers, Ph.D. Associate of Production Malaria Vaccine Development Unit Lab of Parasitic Diseases NIAID, NIH

Discussion of Questions Received

AGENDA (continued)

RFP-NIH-NIAID-DMID-00-18

"MALARIA VACCINE PRODUCTION AND SUPPORT SERVICES"

COLLECT ADDITIONAL TECHNICAL/ADMINISTRATIVE CONCERNS

15 minute break

RESPOND TO:

Additional Technical Questions	Stephanie James, Lee Hall Carol Long, Anthony Stowers
Administrative Questions Negotiation and Award Process	Brenda Velez

12:00 Noon ADJOURNMENT

Malaria Research at NIAID

- Investigator-initiated research grants - *Basic studies (parasite biology, host interaction, vector biology, etc.); SBIRs*
- Solicited research grants and contracts - *international programs, clinical trials*
- Solicited service and support contracts - *reagent supply, vaccine production*
- Capacity strengthening - *Fogarty International Center, Multilateral Initiative on Malaria*
- Intramural laboratories - *basic and translational research, clinical trials*
- Interagency agreements - *access to other government facilities and capabilities*

STEPS IN THE COMPETITIVE ACQUISITION (CONTRACT PROCESS)

(BEGINNING WITH RFP ISSUANCE)

1. RFP ISSUANCE - Request for Proposal (RFP) containing all technical and business requirements is issued. The RFP establishes a specific due date for proposals and provides instructions governing late proposals.

2. PRE-PROPOSAL CONFERENCE (IF NEEDED)

   Pre-proposal conferences may be required in connection with relatively complex contract projects to explain the requirement to potential offerors, and enable them to raise questions concerning any aspect of the requirement before developing their proposals (see FAR 15.409).

3. RECEIPT AND LOG-IN OF PROPOSALS

   Recording the exact time when proposals are received establishes whether they must be considered as late proposals.

4. Technical Evaluation of Proposals

Peer review of proposals is required by 42 CFR 52h and P.L. 99-158, The Health Research Extension Act, 1985.

5. Technical Evaluation Report and Ranking of Proposals

Technical evaluation reports are required by the Executive Secretary as required by HHSAR 315.608-76. The reports include a critique of the technical proposal (strengths and weaknesses) and comments on the reasonableness of judgemental cost factors, when pertinent.

6. Establishment of Competitive Range

The Contracting Officer, after consultation with program officials, makes a competitive range determination based on technical merit, costs, and other factors.

7. Notify Unsuccessful Offerors Determined to be Outside Competitive Range

Offerors determined to be outside of the competitive range are notified in accordance with FAR 15.1001(b), that their proposals will not be considered further.

8. Cost Analysis of Offerors' Proposals

Cost analysis of offeror's proposals is performed by the Contract Specialist and Project Officer in preparation of negotiations with all offerors in the competitive range. This analysis is made in consultation with the Financial Advisory Services Branch of the Division of Contracts and Grants, OD, NIH.

9. Written and/or Oral Competitive Range Discussions

Discussions are conducted with sources in the competitive range to discuss weaknesses and deficiencies in each offeror's technical and cost proposal.

10. Verification of Qualification Criteria

It may be necessary to perform on-site validation of access to the required number of patients.

11. Request for Best and Final Offers

Request for Best and Final Offers are requested for all offerors in the competitive range as described in FAR 15.611 and HHSAR 315.611.

12. Receipt of Best and Final Offers

Request for Best and Final Offers are subject to the same "late proposal" procedures governing initial proposals.

13. Source Selection: Final Evaluation and Recommendations by Source Selection Group

Best and Final Offers may be reviewed by a source selection group composed of some members of the original peer review committee, a program official, an Extramural Activities Program Representative, and Chief, Contract Management Branch, (HHSAR 315.611©).

14. Limited Negotiations with Selected Source

Final touch-up negotiations with selected source(s) may be conducted by the Contract Specialist, if deemed necessary.

15. Preparation of Summary of Negotiation

Negotiation summaries are prepared by the Contract Specialist within the guidelines of FAR 15.808 and HHSAR 315.672.

16. Pre-award Administrative Clearances, as Required, such as Human Subject Assurances and Civil Rights Compliance

Office of Contract Compliance Clearance is specified in FAR Subpart 22.8. Other special pre-award clearances are specified in the acquistion regulations and DHHS or NIH Manual Systems.

17. Pre-award Review by NIH Board of Awards or Institute Reviewer Depending on Dollar Value

Pre-award reviews are required within the DHHS to ensure the contract awards are in conformance with law, established policies and procedures and sound business practices, and that contractual documents reflect mutual understanding of the parties. (HHSAR Subpart 304.71.)

18. Award

Award is accomplished for negotiated contracts after execution by both parties.

19. Notification to Unsuccessful Offerors

Notification of awards made will be provided to all unsuccessful offerors. (Notification and debriefing procedures are specified in FAR 15.1001, 15.1002, 15.1003, and HHSAR 315.1003.)

20. Conduct Debriefings for Unsuccessful Offerors as Requested

Upon written request from unsuccessful offerors, the Contracting Officer will provide details of weaknesses and deficiencies of their proposals. (Detailed debriefing requirements are contained in HHSAR 315.1003).

21. Postaward Orientation (if needed)

Postaward conferences are sometimes held with the successful Contractor(s) (as described in FAR 42.503) to ensure that the Contractor has a thorough understanding of performance requirements (usually held in connection with more complex contracts).

22. Postaward Administration

The postaward administration phase conists of many individual and continuous tasks including technical surveillance, thorough review of financial management reports by the Project Officer and Contracting personnel (likewise review of the Contractor's periodic vouchers), review of progress reports, periodic site visits as required, etc.

Technical Monitoring
Progress Report Analysis
In-Process Reviews
Financial Surveillance
Site Visits
Acceptance of Final Comprehensive Report as Contract End Product

23. Closeout Phase

The contract closeout phase entails final audit and reconciliation of costs under a cost-reimbursement type contract before payment of the Contractor's final voucher. Final payment is also predicated upon receipt of final technical reports, property inventories, patent disclosure reports, etc. This process is described more fully in FAR 4.804-5 and HHSAR 304.804.

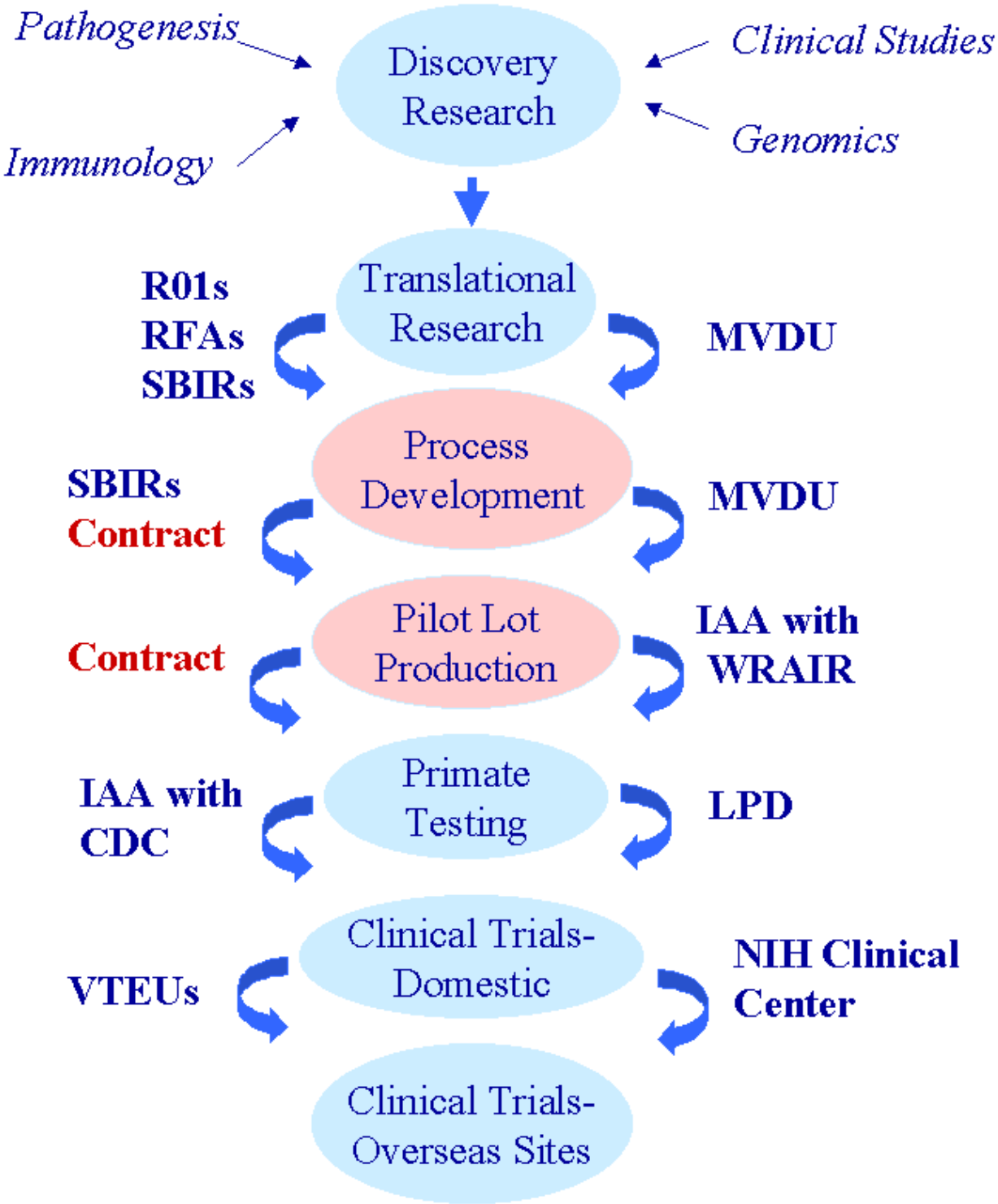
The NIAID Research Plan for Malaria Vaccine Development

- **GOAL: To accelerate research leading to the development of a vaccine to reduce the mortality and morbidity resulting from malaria**
- HIGHLIGHTS:
  - Improved access to well characterized research materials
  - Discovery and preclinical testing of vaccine candidates
  - Production and evaluation of candidate malaria vaccines
  - Clinical research and trial preparation sites in endemic areas

NIAID Plan Timeline

- **1997 - NIAID Research Plan for Malaria Vaccine Development** (http://www.niaid.nih.gov/dmid/malvacdv/toc.htm)
- **1998 - Human Immune Response in Endemic Areas**
- **1998/99 - Malaria Research and Reference Reagent Resource Center** (http://www.malaria.mr4.org/mr4pages/index.html)
- **1999/00 - Clinical Research and Trial Preparation Sites in Mali and Ghana**
- **2000 - Enhancing Vaccine-elicited Protective Immunity in Malaria**
- **2000 - Malaria Vaccine Production and Support Services**

Development Pathway at NIAID



2) Record of Pre-Proposal Conference on October 22, 1999

Record of Pre-proposal Conference

RFP-NIH-NIAID-DMID-00-18

A pre-proposal conference for RFP-NIH-NIAID-DMID-00-18 was held on October 22, 1999, at 6700B Rockledge Drive, Room 1205, Bethesda, Maryland. The purpose of the conference was to provide information concerning the above mentioned RFP and to answer any questions potential offerors might have regarding this acquisition and the proposal preparation, evaluation and award process.

Ms. Brenda Velez, Chief, Contract Management Branch (CMB), opened the pre-proposal conference at 9:00 a.m. Ms. Velez introduced Ms. Nancy Hershey, the CMB staff member who will be responsible for this RFP. Ms. Velez also introduced the NIAID Program Staff who would be responsible for this acquisition: Dr. Stephanie James, Dr. F. Benton (Lee) Hall, Carole Long, and Anthony Stowers. Ms. Velez gave a brief introductory overview of the format for the conference and an overview of the contract acquisition process.

Stephanie James, Ph.D., Chief, of the Parasitology and International Programs Branch, Division of Microbiology and Infectious Diseases, NIAID, NIH, then took the floor and presented an overview of the NIAID Malaria Vaccine Development program. F. Fenton Hall, M.D., Ph.D., Project Officer for the Parasite Vaccine Program, Parasitology and International Program Branch, Division of Microbiology and Infectious Diseases, NIAID, NIH, then took the floor and presented an overview of this RFP for the NIAID Malaria Vaccine Production and Support Services.

Written answers to written questions which had been received by CMB as of October 22, 1999, were then presented and discussed by Ms. Stephanie James.

There was a 15 minute break after which additional technical and administrative questions from conference attendees were addressed by Dr. Stephanie James, Dr. F. Benton Hall, Carole Long, Anthony Stowers, and Brenda Velez. Ms. Velez stated that these additional questions along with written questions and answers reviewed and distributed would be furnished in writing to all prospective offerors whether or not they attended the conference.

Competitive Acquisition Process

Ms. Brenda Velez,

CMB issued RFP NIH-NIAID-DMID-00-18 entitled “Malaria Vaccine Production and Support Services" on September 15, 1999. The due date for receipt of proposals is January 14, 2000.

The Competitive Acquisition (Contract) Process consists of multiple steps. The technical evaluation of proposals is under the purview of the Scientific Review Program (SRP) of the NIAID, which is entirely distinct from Program Staff. A group of individuals with expertise in the RFP’s subject matter (peer review committee) is responsible for evaluating the technical proposals submitted to the Institute. The evaluation criteria delineated

in the RFP are used as a measure for evaluating the proposals and for determining how well the offerors' develop their technical approaches. Proposals receive a numerical score following evaluation and are ranked as acceptable or unacceptable. The next step of this process involves establishing which proposals will be considered in the "Competitive Range". Only offerors whose proposals lie within this competitive range have the opportunity to receive an award. After the competitive range is established, offerors whose proposals are not in the competitive range will be notified.

As stated in the RFP, CMB requests two types of proposals from offerors, a technical proposal and a business proposal. The peer review committee evaluates the technical proposal; CMB evaluates the business proposal, in consultation with auditors, to ascertain that all cost information submitted with the proposal is accurate and correct.

CMB will conduct technical and cost/adminstrative negotiations with offerors whose proposals are in the competitive range. CMB verifies the qualifications of each institution, and requests a Final Revised Proposal (formerly called the Best and Final Offer) from each offeror whose proposal is in the competitive range. After receiving the proposals, CMB convenes a Source Selection Group. This Group consists of two of the original reviewers from the initial peer review group, the project officer, the Director of the DEA (or his designee), and the Chairperson of the CMB (as a non-voting chair). This Group evaluates the final proposal based on the offerors' responses to questions asked during the negotiations process. The Source Selection Group will re-score the proposal based on the offerors' responses to initial concerns of the peer review committee using the technical evaluation criteria included in the RFP. During negotiations, issues identified by peer reviewers will be brought to the offerors' attention and re-evaluated at the Source Selection Group meeting. At the Source Selection Group meeting, CMB will select the awardee of the contract, taking into consideration all factors of the technical evaluation criteria in order of importance. Although technical factors are of paramount consideration in the award of the contract, cost/price are also important to the overall contract award decision. CMB will notify the awardee if some minor or minimal issues need to be addressed. These issues, however, would always be sufficiently minor and would not affect the selection process.

Before awarding a contract, CMB prepares the summary of negotiations, the contract, and prepares the contract file for a series of reviews. Pre-award clearances must be obtained before issuing the final award. Once the contract has been awarded, CMB will notify unsuccessful offerors of the organization(s) who received an award. Unsuccessful offerors may request a debriefing of their proposal with the CMB.

General Overview of Malarial Program

Dr. Stephanie James

The RFP-NIH-NIAID-DMID-00-18 ("Malaria Vaccine Production and Support Services") can be placed in context with other programs that the Institute is establishing under its Malaria Vaccine Development Plan. Within the past few years, the Institute has substantially increased its malaria research effort. This effort is occurring within the Division of Microbiology and Infectious Diseases' (DMID's) extramural program, Parasitology and International Programs Branch, which supports malaria research conducted in other institutions nationwide and around the globe, and within the Division of Intramural Research (Laboratory of Parasitic Diseases). (Dr. Carole Long and Dr. Anthony Stowers, represent the intramural component of the Institute at this pre-proposal conference.)

The Institute supports malaria research using a variety of different mechanisms. The major component of the extramural program is investigator-initiated research that is funded by RO1s, or other types of R grants. These

investigator-initiated grants generally involve basic research, on topics such as parasite biology, host-mosquito interaction, or vector biology. The Institute also considers Small Business Innovative Research (SBIR) grants as investigator initiated research grants that support more developmentally-oriented research.

Solicited research grants and contracts are used to support more targeted or directed programs of interest to the Institute. For example, all collaborative international research programs are conducted under these funding mechanisms, as are most clinical trials. Solicited service and support contracts provide reagents and services; two of these contracts are particularly relevant to the malaria program. One is a new contract to provide malaria reagents to the research community; this significant contract was awarded to the American Type Culture Collection. The new vaccine production contract, which is the subject of this RFP, is likewise considered in the category of a solicited service and support contract.

The Institute conducts research and clinical trial capacity strengthening activities under a number of mechanisms, including NIAID solicited programs, as well as interaction with the Fogarty International Center and the World Health Organization (WHO) as part of its role as in the Multilateral Initiative on Malaria (MIM). Thus, the Institute is involved in malaria research in a number of countries where the disease is endemic. NIAID's intramural laboratories conduct research activities and clinical trials at the Bethesda campus and the Malaria Research and Training Center in Mali. The Institute also uses inter-agency agreements (IAAs) to gain access to facilities and capabilities that are present within other government agencies.

In 1997, at the beginning of developing the Multilateral Initiative on Malaria, Dr. Anthony Fauci requested the extramural and intramural programs to develop a joint research plan for malaria vaccine development. That plan is currently available on our NIAID website, and is mentioned in the introduction to the RFP. The plan was vetted through a panel of external experts. The goal of the plan was defined as the acceleration of research leading to the development of a vaccine that would reduce the morbidity and mortality resulting from malaria. The highlights of that plan included the following: a) to improve access to well characterized research materials for the entire research community; b) to increase the discovery and testing of vaccine candidates in preclinical testing/models; c) to increase the ability to produce and evaluate candidate vaccines in the clinic; and d) to establish research and clinical trial preparation sites in endemic areas so clinical trials could be conducted in regions where malaria transmission occurs.

Implementation of the NIAID plan has encompassed a number of initiatives. The Institute has awarded a series of cooperative agreements to study protective immune responses in individuals who live in areas where the disease is endemic. A major contract was awarded to establish the Malaria Research and Reference Reagent Resource Center (MR4). In late 1998 and in early 1999, two contract awards involving Mali and Ghana, were made for research and clinical trial preparation sites. In the near future, the Institute will award several grants to investigators for research to enhance vaccine-elicited protective immunity in malaria. The NIAID intramural laboratories are creating a Malaria Vaccine Development Unit (MVDU). With the award of this contract at the end of the current fiscal year, all programs outlined in the Malaria Plan of 1997 will have been established.

The NIAID hopes to establish a development pathway for malaria vaccines at NIAID that will take advantage of the large body of investigator-initiated basic and discovery research that is supported by the Institute. NIAID will utilize available extramural mechanisms and intramural capabilities to support translational research. The capability for process development will be enhanced through this contract as well as the MVDU. Capacity for production of pilot lots of clinical grade vaccines will be provided through this contract as well as an IAA with the Walter Reed Army Institute for Research. The Institute is evaluating its capacity for candidate vaccine testing in primates; the intramural laboratories already have some capacity for these studies, and an IAA with the CDC is under negotiation to further expand this capacity. The Institute has the capacity to conduct domestic

clinical trials both at the NIH Clinical Center and through the Vaccine and Treatment Evaluation Units (VTEU), a series of contracts held by DMID at a number of universities across the country. Finally, NIAID is developing the capacity to conduct clinical trials at overseas sites where malaria is endemic. It is clear that the contract to be be awarded under this RFP occupies a crucial control position in this development pathway for malaria vaccines.

Technical Aspects of the RFP

Dr. Lee Hall

The Institute anticipates making one award for this contract. The Scope of Work of the proposed contract involves a number of diverse tasks, and specifically mentions that subcontracting will be permitted. The contract will be a cost-reimbursement, completion-type contract with an expected duration of 7 years.

The contract addresses four areas including: 1) project management support for the development of lead malaria vaccine candidates; 2) process development services for candidate malaria vaccines; 3) pilot lot production; and 4) regulatory support. As discussed by Dr. James, this contract is expected to fill a "niche" in the Institute's overall malaria plan; each of the four areas of the contract will address part of that niche. The technical evaluation criteria (factors) are listed at the back of the RFP. In terms of the technical proposal, it is useful to look at the relative weighting of factors. Obviously, the majority of the weight is given to the Technical Approach, which accounts for 60% of the final score. Personnel qualifications account for 30% of the final score, (research and administrative, 20% and 10%, respectively); and, facilities and resources account for 10% of the score.

In terms of project management support, the malaria program is looking for the following aspects: 1) to organize and support the meetings of various advisory groups, including the Malaria Vaccine Task Force; 2) to address intellectual property issues related to particular vaccine candidates; 3) to provide project managers to organize and orchestrate the project management process for a particular candidate vaccine; 4) to organize a product development team, which is expected to include scientists involved in the initial identification of the candidate vaccine, individuals involved in production, and individuals with expertise in regulatory affairs. (This product development team would be based on a model similar to that adopted by industry); and, 5) to integrate the project planning and management activities of these particular areas. Details of these general categories are described within the RFP.

With regard to process development, DMID expects that a project plan will be developed for each vaccine candidate that will include appropriate aspects of process development. Process development will also include optimization of immunogen production, in-process QA and QC assays, optimization of product recovery, purification, characterization, and evaluation for subsequent pilot lot production. Written standard operating procedures (SOPs) will be required for each pilot lot production. These requirements are designed to expedite the process of vaccine development to pilot lot production.

The RFP focuses on 5 production categories of candidate vaccines, including: 1) recombinant proteins expressed in prokaryotic systems; 2) recombinant proteins expressed in eukaryotic systems; 3) vector-based vaccines in bacterial or viral systems; 4)synthetic peptides; and 5) nucleic acid vaccines. For responding to the process development portion of the RFP, offerors must provide evidence of possessing the technical expertise and having access to facilities necessary to produce "an exemplary vaccine candidate produced in two eukaryotic expression systems (e.g, a mammalian cell expression system and a non-Saccharomyces eukaryotic expression system), in addition to a vector-based vaccine candidate. (see the RFP for specific requirements).

In the area of pilot lot production, offerors must provide detailed production and budget plans for preparation of a GMP grade Master-Stocks, (where applicable), and eventual production of clinical grade product, including formulation, vialing, labeling, packaging, storing and shipping, testing for release specification criteria (including pyrogenicity testing,) stability and immunogenicity testing, and support of appropriate data for an IND submission.

For pilot lot production, the technical proposal requires that offerors provide specific information on an abbreviated validation master plan, evidence for access to GMP production capability, a process for identification of additional facilities and expertise as needed; and budgets for each category based on a gram of protein or peptide vaccine, and 2000 doses of vector-based vaccine and 2000 doses of a DNA vaccine.

In terms of regulatory support, the successful offeror must be capable of preparing, updating, and distributing the Investigator's Brochure, preparing a Master File, collecting and submitting documentation for IND submission, assembling the IND study protocol, and assembling labeling and indexing IND submissions. In addition, the offeror must obtain appropriate authorization for cross-filing, (when appropriate), and preparing an environment assessment, if required.

Reporting requirements are rather straightforward and include monthly status reports that can be sent to the project officer via e-mail, written quarterly reports, and a final report. Other deliverables at the completion of the contract include the vaccine candidates in various stages of development, a complete listing of accurate and updated information on the design, development, production of a candidate vaccine at termination of the contract, and a complete listing of information on the regulatory support activities of the Contractor and any Government owned property or equipment accumulated during the course of the contract. Further details on all aspects of these requirements are provided in the RFP.

Malaria Vaccine Development Unit/Laboratory of Parasitology

Dr.Carole Long

The Malaria Vaccine Development Unit (MVDU) is a component part of the Laboratory of Parasitic Diseases at NIAID. The Unit is headed by Dr. Louis Miller, who is also the Chief of the Laboratory of Parasitic Diseases. The MVDU is comprised of three major units:

- Immunology Unit; Dr. Carole Long , Head;
- Expression of Recombinant Protein and Process Development Unit; Dr. Anthony Stowers (Acting Head); recruitment is in progress for the Head of this unit.
- Clinical Trials Unit; Dr. A. Magill, Head (as of January, 2000). Dr. Magill will be head the clinical trials conducted at the NIH Clinical Center, and will be involved in clinical trials conducted at other domestic and foreign sites.

These three major components of the MVDU are located principally at the Institute's Twinbrook Facility; however, some individuals are located at the NIH Main Campus. The facilities at Twinbrook, which are currently under renovation for a group of 20-25 individuals, will have new laboratory components for immunology, fermentation and process development. These laboratories will be GLP, not GMP, facilities. In addition, the MVDU is collaborating with other groups, including a small number of contracts or CRADAs.

The MVDU has access to a NIAID animal facility in Poolesville, Maryland, which houses Aotus monkeys. The candidate vaccines of interest to MVDU vary considerably in their stage of development; some of these

candidates are still being evaluated in basic research laboratories, while others are at an intermediate stage of development or are close to IND submission. In general, the MVDU will focus on recombinant antigens produced in bacteria and yeast.

A copy of these minutes will be made available to all attendees of today's meeting, as well as any potential offerors on the RFP website. Thus, CMB will ensure that all information discussed at the conference is equally available to everyone who is interested in submitting a proposal in response to the RFP.

2) Questions and Answers Concerning the RFP (received prior to the pre-proposal conference on October 22, 1999)

RESPONSES TO QUESTIONS FROM POTENTIAL OFFERORS

RFP NIH-NIAID-DMID-00-18
"MALARIA VACCINE PRODUCTION AND SUPPORT SERVICES"

The responses to the technical questions have been prepared for this pre-proposal conference. The questions are stated followed by NIAID's response.

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1. Is the Contractor restricted from usage of company–owned proprietary properties and/or processes in fulfillment of the contract's objectives?

   If the Contractor during the course of this contract makes intellectual inventions on the malarial vaccines, please explain the process for an agreement between the Office of Technology Transfer (NIH) and the Contractor and what are the limitations?

   RESPONSE: No. The rights of the contractor will be protected in the same way as indicated for a third party inventor under Work Statement Attachment 1, "Protection of Proprietary Data". If the contractor makes an invention under the contract, under the Bayh-Dole Act they own that invention.

2. Can the Contractor propose alternate methods for safety and analytical testing stated in the RFP?

   RESPONSE: For purposes of technical evaluation, all proposals should respond to the requirements of the Work Statement. Alternative or additional methods may also be proposed, or may be suggested by the contractor at any time in the development process.

3. Will the final container products produced in the pilot production be used in phase II clinical studies?

   RESPONSE: **We anticipate that this will be the case if Phase I studies indicate that Phase II should be pursued.**

   If so, will the Contractor be able to interact with those researchers involved in the clinical studies?

   RESPONSE: **The preclinical development team organized by the contractor (see Part 1.d. of the Work Statement) may contain one or more individuals involved in planning subsequent clinical studies, particularly when the candidate has proceeded to pilot lot production. The contractor may also be included on the clinical development team involved in planning/conducting clinical trials. During clinical trials, however, the contractor will not have the oversight and organizational responsibilities described in this RFP for preclinical studies.**

4. Does the proposal require the inclusion of a list of prototype SOPs for production of each type of vaccine?

RESPONSE: **Yes, see Note 4 to Offeror: "For purposes of responding to this RFP, the Offeror should provide evidence of access, either directly or through subcontracting, to technical expertise and facilities capable of providing the required services for one exemplary vaccine candidate from each of the five categories, including a sample SOP."**

5. Do SOPs for each analytical and safety test performed by QC need to be in the proposal?

   RESPONSE: **See Note 3 to Offeror: "In each case, include: a description of the anticipated development milestones; generalized protocols for vaccine production, purification and immunogenicity testing; and, documentation of experience in meeting such milestones in a timely manner." Offeror should provide generic protocols sufficient to document "technical expertise and facilities capable of providing the required services for an exemplary vaccine candidate produced in two eukaryotic expression systems, (one of which must be mammalian cells, and another system excluding Saccharomyces), and a vector-based vaccine candidate." It is anticipated that detailed SOPs can only be developed for specific vaccine candidates, and that this will be done on a case-by-case basis after the contract is awarded.**

6. Would you clarify the number of vaccine candidates put into the pipeline each year for R&D and for pilot production?

   RESPONSE: **It is anticipated that no more than 3 candidates will be considered for pilot production in Year 1 and no more than 6 will be considered for pilot production in each of the subsequent years (see Note 4 to Offeror). The number of candidates in process development may differ, and is difficult to predict at this time. As stated in Note 3 to Offeror, "for budgetary purposes, assume one candidate/year will be designated for process development from each of the five categories." The number of candidates at any stage of development will be negotiated on an ongoing basis with the Project Officer.**

7. Please define the initial growth studies stated on page 7 (d) of the RFP.

   RESPONSE: **This language refers to growth of the organism producing a recombinant protein (e.g. bacteria, yeast, or insect cells infected with recombinant baculovirus).**

8. Will final CMC reports used in IND submissions suffice as evidence of submissions to CBER/FDA?

   RESPONSE: **Yes. As stated in Note 5, the Offeror may provide anything that constitutes evidence of previous experience with submissions to CBER.**

   Do you need the IND numbers?

   RESPONSE: No
   If so, confidentiality of these documents must be maintained and sanitization may be required due to contractual relationships between clients and contractors.

9. Will the Contractor meet with NIH scientists that work on malaria on a weekly schedule?

   RESPONSE: Minimum reporting requirements to the NIAID Project Officer are described in Attachment B. As described in Part 1.d. of the Work Statement, the contractor will establish a team of scientists (which may include NIAID intramural or NIAID-supported extramural scientists, as well as others possessing relevant expertise) to help with process development and/or pilot lot production for each malaria vaccine candidate, and work with this team as needed.

10. What is the quantity of recombinant protein required for each final bulk product made in pilot production?

    RESPONSE: **As stated in Note 4 to Offeror, the estimated quantity of recombinant protein will be 1 gram. This may vary according to the individual candidate.**

    How many final container vials will be needed for each protein vaccine?

    RESPONSE: As indicated in Note 4 to Offeror, the anticipated need is for approximately 2000 doses of vaccine. It is expected that this will <u>not</u> be packaged in single-dose vials. Moreover, at the time of initial vialing, some material may remain stored as bulk product.

11. Please define a dose for the recombinant viral and bacterial expression systems and for DNA vaccines.

    RESPONSE: It is the intent of this RFP to provide a capability for producing a variety of different vaccine candidates. Until the individual candidate is identified and has undergone preclinical immunogenicity testing as well as dose ranging in clinical studies, it is difficult to estimate the final dose per immunization. At this time, it is estimated that the dose for potential vaccines to be produced under this contract will fall within the range of doses reported in prior publications for similar malaria vaccine candidates.

12. Does R&D of vaccine candidates proceed through all seven years of the contract?

    RESPONSE: Yes

13. Can equipment used on this project solely be replaced if a need arises or a replacement is needed? (eg. ultralow freezer).

    RESPONSE: Yes. This will be negotiated with the Project Officer on a case-by-case basis.

14. Is a government-funded entity outside of the US eligible to submit a proposal for the RFP for Malaria vaccine production and support services?

    RESPONSE: Yes. This RFP is for "full and open competition" for all parties. All interested parties may apply. Your proposal will be evaluated in accordance with the technical evaluation criteria listed in the RFP.

15. Is a private institution outside of the continental USA eligible to apply?
RESPONSE: Yes. See the answer to #14 above.

16. The Statement of Work calls for 4 major service areas including project management, process development, pilot production and regulatory support. Will a proposal be considered complete only if the interested party covers all four services in the submission? OR could a potential contractor request to furnish work for one to two parts alone?

RESPONSE: A response to all four parts is required. If a potential offeror is not equipped to provide all 4 components, it should consider forming a consortium arrangement with others who could complement its qualifications. In Note 1 to Offeror, the RFP specifically states that subcontracting is allowed, but in that case the Prime contractor must have demonstrated experience in project management.

Responses to Questions Proposed by Potential Offerors at the pre-proposal conference on 10/22/99

1.Will NIAID entertain and consider the use of other vaccines and technologies, for example, the use of edible vaccines.

RESPONSE: The Institute would certainly be interested in knowing about such vaccines and alternate technologies, and would like to be made aware of them through the RFP. In terms of responding to the RFP itself, however, offerors will be evaluated solely on the criteria outlined in the RFP. The SOW, as specified in the RFP and technical evaluation criteria (TEC), could allow offerors to submit alternate approaches outside the specified and required area; but offerors will not be evaluated on these alternate approaches to vaccine development and formulation. The evaluation criteria are contained within the RFP, and offerors would be first evaluated on requirements specified in the SOW. Ultimately, however, NIAID is interested in establishing a team structure, in which the Institute will listen to contractors' new ideas and better alternatives, etc, throughout the course of the contract. In addition, the scope of work is substantial, so a fair amount of flexibility will be required. Offerors should consider these issues when preparing their proposals.

2. The Scope of Work appears to place heavy emphasis on broad project management, regulatory management, and experience in an exceptionally wide range of production. But the scoring in the technical evaluation criteria appears to stress heavy emphasis on production. Is this assessment accurate?

RESPONSE: When reading the technical evaluation criteria, offerors must consider that management capability is addressed in both the Technical Approach and Personnel Qualifications. Since DMID is a small division with a large work effort, it has a strong need for a contractor with management capability and experience. DMID requires that the successful offeror will have excellent management skills and experience, and a demonstration of these management qualities is a critical part of the Evaluation Criteria and scoring. These management capabilities, however, should be made obvious in the offeror's description of how the 4 areas (project management, process development, pilot lot production and regulatory) will be addressed in furthering production and development of candidate malaria vaccines.

3. An offeror with industry or biotechnology experience or someone coming out of industry or biotechnology may need to collaborate with other individuals or institutions that have established experience in malaria research. Does the RFP allow for this possibility?

RESPONSE: Such collaborations are certainly expected and the RFP includes a potential role for subcontractors in this contract. It is anticipated that teams of scientists will work together on these projects. DMID expects that for any given vaccine candidate these teams will include scientists who are experienced in conducting malaria research. The idea of teams of scientists working together is certainly taken into account with the subcontracting option identified in the RFP. For any given candidate, those teams might include, for example, people very familiar with carrying out immunogenicity testing and biological activity testing of particular candidates. These types of studies can be conducted adequately by subcontractors.

4. In regards to listing your requirements for project management, I find it difficult for a biochemist to obtain project management experience in a small biotechnology facility, but this experience is easily obtained in software companies. (I took courses in Silicon Valley). Is there a way to clarify how an applicant acquired project management skills?

RESPONSE: That information should be included in the Technical Approach and can be provided in the section on qualifications and criteria of personnel. The offeror might list or describe the management experiences of certain essential personnel and outline how individuals will function as a team. Offerors must remember that the peer reviewers will only be using information provided in the proposal when evaluating whether an offeror possesses the requisite skills and experience stipulated in the technical evaluation criteria. Also, consider the RFP's Note 1 to offerors that states that offerors shall describe an administrative framework and the clear lines of authority of staff bid on the contract. This description is important for evaluating project management experience.

5. Will any of the candidate vaccines from this contract be tested in lower malaria models; (i.e., preclinical models)? If so, which models will be used in these studies?

RESPONSE: Vaccines will be tested in any model that is best to evaluate their activity. Intramural facilities that are available can be accessed for this testing. Extramural investigators or other programs are also capable of conducting these additional evaluations. The DMID Malaria Program is charged with the responsibility of finding capacities that can contribute to effort. In terms of preclinical testing, there are obviously some generic aspects that must be addressed; specialized companies are available that can bid for funds to conduct these preclinical evaluations.

6. Who will select the candidate vaccines evaluated in this project?

RESPONSE: DMID is interested in the input of the entire malaria research community in selecting the most appropriate vaccines as "candidates". However, the Project Management Section in Part B of the RFP clearly states that the project officer will select candidate vaccines to be evaluated in this contract.

7. Would it be helpful to propose an "active surveillance" effort for new vaccine technologies as part of the response to the RFP?

RESPONSE: This is not specifically called for in the RFP, although it might be covered under project management activities described in parts 1.d and 1.f of the Work Statement. NIAID will be seeking to make use of the most appropriate available technology during the course of this seven year contract, and, as discussed under Question 9, will certainly value the recommendations of the contractor as part of the scientific team(s) working together on an ongoing basis to optimize process development and pilot lot production.

The pre-proposal conference adjourned at 10:30 a.m.

2) List of Attendees at Pre-proposal conference on October 22, 1999

Attendees

Science Applications International Corporation
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(301) 698-5991

Donna L. Bareis, Ph.D., Corporate Vice President, Dr. Walter Brandt, Dr. William Bancroft, Dwight Wolfe, Ms. Florence Kaltovich

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Dr. Marie Reeves, Dr. Christopher Kemp

BioScience Contract Production Group
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Gan Wei

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Dr. Vittoria Cioce, Robin A. Robinson, Ph.D., Associate Director

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Dr. Joseph Sinkule, President and CEO

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Contracts Management Branch
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Contracts Management Branch
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Joel Campbell, Ph.D.
Contractor; (LTS)

Madelon Halula, Ph.D.
Chief, Special Review Branch
Scientific Review Administrator
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Anna Ramsey-Ewing, Ph.D.
Scientific Review Administrator
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